

SHORT REPORT

Nitrate in community water supplies and incidence of non-Hodgkin's lymphoma in Sardinia, Italy

P Cocco, G Broccia, G Aru, P Casula, S Muntoni, K P Cantor, M H Ward

J Epidemiol Community Health 2003;57:510-511

Studies of non-Hodgkin's lymphoma (NHL) evaluating risk associated with nitrate concentrations in community water supplies have found inconsistent results.¹⁻⁴ To further explore this hypothesis, we compared the NHL incidence in 1974-1993 with nitrate monitoring data from 1971-1994 available for 75% (282 of 376) of the communes (administrative units) in Sardinia, Italy.

METHODS

We selected the 153 communes with at least one nitrate measurement in 1993 or earlier (median: 5 measurements; range: 1-51) after excluding the six major urban areas. The population of these 153 communes ranged from 140 to 61 636 (median: 2459) and included a population of 703 000 (41% of the Sardinian population). There were a total of 3909 nitrate measurements. The nitrate ion was measured by spectrophotometry with the sodium salicylate method. For our primary analysis, we used the average nitrate concentration in 1993 as the exposure metric. Fifteen communes (23% of the study population), also had nitrate data in 1971-84. For these we also evaluated the median concentration in 1971-84. NHL incidence in 1974-1993 was determined by commune from the registries of all pathology and haematology departments in Sardinia. Coverage of these registries was estimated as close to 100%.⁵ We calculated person years for each gender group and 10 year age group in each commune, using the 1971, 1981, and 1991 census enumerations, extended five years backward and four years onward. We aggregated cases and person years over all communes within eight categories of 1993 nitrate level. Incidence rate ratios (IRR) and 95% confidence intervals for NHL were computed for each nitrate category with reference to the lowest using Poisson regression, and adjusting by gender, age, and population size.

RESULTS

Among the 153 study communes, the average nitrate concentration in 1993 was 4.57 mg/l (SE 0.35; median: 3.27). The IRRs for NHL for both genders combined did not increase with

increasing 1993 nitrate level (table 1). Among men, the IRRs were significantly increased in some nitrate concentration categories, but no linear increase was observed (χ^2 for trend=3.25; 0.10>p>0.05). Among women, the IRRs were not increased in any exposure category. The results did not change using different exposure categories cut off points, and results were similar for the NHL incidence in 1974-83 and in 1984-93. Among the 15 communes with monitoring data in 1971-84, the median nitrate concentration was 8.11 mg/l (IQR 4.42-24.34), and it was significantly correlated with the 1985-1994 median ($r=0.577$; $p<0.05$), and with the 1993 level ($r=0.613$; $p<0.05$). Nitrate concentrations in 1993 were substantially lower in these 15 communes (median: 4.10; IQR 2.91-8.06) compared with the 1971-84 median concentration, and the IRRs for NHL were increased 2-fold to 2.5-fold for increasing quartile of nitrate concentrations compared with the lowest. The risk increase was consistent by gender. Still, no significant upward trend was observed. However, the incidence rate in the reference category was based only on seven cases and 116 778 person years and when the reference category was extended to <8.0 mg/l nitrate, the IRR was 1.3 for 8-24.9 mg/l, and 1.0 for ≥ 25 mg/l. Finally, we repeated the analyses in table 1 after excluding these 15 communes. This resulted in a reduction of the raised IRRs for NHL. Only one AIDS related NHL case occurred among the 737 NHL cases observed in our study population. Therefore, we can reasonably exclude that the urban/rural gradient of AIDS related NHL might have significantly affected our findings.

COMMENT

We found limited evidence among men but not women of an association between NHL incidence and nitrate concentrations in community water supplies. Low average concentrations, exposure misclassification, and the limitations of the ecological design might account for our results. Further studies with historical monitoring data, individual estimates of exposure, and information on potential confounders are

Table 1 Relative risks (and 95% confidence intervals) for non-Hodgkin's lymphoma and 1993 nitrate concentration in community water supplies for the total population and by sex

Nitrate concentration (mg NO ₃ -/l)	Total			Men			Women		
	Cases	P-Y	IRR (95% CI)	Cases	P-Y	IRR (95% CI)	Cases	P-Y	IRR (95% CI)
≤2.0	113	1301554	1.0	46	638266	1.0	67	663288	1.0
2.01-3.0	119	1270287	1.13 (0.87 to 1.47)	57	627826	1.29 (0.87 to 1.92)	62	642461	1.02 (0.71 to 1.45)
3.01-4.0	94	896781	1.21 (0.91 to 1.61)	56	444334	1.70 (1.13 to 2.56)	38	452447	0.86 (0.56 to 1.30)
4.01-5.0	138	1398393	1.15 (0.88 to 1.49)	71	686981	1.42 (0.96 to 2.10)	67	711412	0.95 (0.66 to 1.37)
5.01-7.0	103	1242462	1.01 (0.76 to 1.33)	62	604807	1.46 (0.99 to 2.16)	41	637655	0.69 (0.46 to 1.03)
7.01-10.0	46	376247	1.40 (0.99 to 1.99)	28	184715	1.98 (1.23 to 3.20)	18	191532	0.98 (0.57 to 1.66)
10.01-15.0	91	953026	1.0 (0.74 to 1.36)	54	454833	1.45 (0.95 to 2.22)	37	498193	0.69 (0.44 to 1.07)
15.01-26.64	33	317724	1.32 (0.88 to 1.97)	17	157409	1.64 (0.92 to 2.91)	16	160315	1.10 (0.63 to 1.93)

needed to adequately evaluate the hypothesis that NHL risk is associated with increased nitrate concentrations in drinking water.

.....

Authors' affiliations

P Cocco, G Aru, Department of Public Health, Occupational Health, University of Cagliari, Italy

G Broccia, P Casula, Division of Haematology, Oncology Hospital, ASL 8, Cagliari, Italy

S Muntoni, Department of Biomedical Sciences and Biotechnologies, University of Cagliari

K P Cantor, M H Ward, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, USA

Funding: none.

Conflicts of interest: none.

Correspondence to: Dr P Cocco, Department of Public Health, Occupational Health Section, University of Cagliari, via San Giorgio 12, 09124 Cagliari, Italy; coccop@pacs.unica.it

Accepted for publication 8 November 2002

REFERENCES

- 1 **Weisenburger DD**. Potential health consequences of ground-water contamination by nitrates in Nebraska. In: Bogardi I, Kuzelka RD, eds. *Nitrate contamination*. NATO ASI Series. Vol G 30. Berlin: Springer-Verlag, 1991:309–15.
- 2 **Ward MH**, Mark SD, Cantor KP, *et al*. Drinking water nitrate and the risk of non-Hodgkin lymphoma. *Epidemiology* 1996;**7**:465–71.
- 3 **Weyer PJ**, Cerhan JR, Kross BC, *et al*. Municipal drinking water nitrate level and cancer risk in older women: the Iowa Women's Health Study. *Epidemiology* 2001;**12**:327–38.
- 4 **Law G**, Parslow R, McKinney P, *et al*. Non-Hodgkin's lymphoma and nitrate in drinking water: a study in Yorkshire, United Kingdom. *J Epidemiol Community Health* 1999;**53**:383–4.
- 5 **Broccia G**, Cocco P, Casula P. Incidence of non-Hodgkin's lymphoma and Hodgkin's disease in Sardinia, Italy: 1974–1993. *Haematologica* 2001;**86**:58–63.

Journal of Epidemiology and Community Health through the ages

Browse the Archive

Journal of Epidemiology and Community Health online has an archive of content dating back to 1978.
Full text from January 2000; abstracts from 1978; table of contents from 1978

www.jech.com